

REMARKS

Claims 1-38 were pending the application. Claims 1, 3-7, and 34 have been amended. Accordingly, upon entry of this amendment, claims 1-38 will remain pending. For the Examiner's convenience, the pending claims are set forth in Appendix A.

Support for the amendments to claims 1, 3-7, and 34 may be found throughout the specification, including the originally filed claims.

No new matter has been added. Any amendments to the claims was done solely to more particularly point out and distinctly claim the subject matter of Applicants' invention in order to expedite the prosecution of the application. Applicants reserve the right to pursue the claims as originally filed in this or a separate application(s).

Election/Restriction

The Examiner has required restriction to one of the following inventions under 35 U.S.C. §121:

- | | |
|------------|--|
| Group I: | Claims 1-17, drawn to an isolated nucleic acid, vector, host cell, and method of making a polypeptide, classified in class 435, subclass 69.1. |
| Group II: | Claims 18-24, drawn to an isolated polypeptide, classified in class 514, subclass 2. |
| Group III: | Claims 25-33, drawn to methods producing a fine chemical comprising culturing a cell containing a vector, classified in class 435, subclass 41. |
| Group IV: | Claim 34, drawn to a method for producing a fine chemical comprising culturing a cell whose genomic DNA has been altered by inclusion of a nucleic acid, classified in class 435, subclass 41. |
| Group V: | Claim 35, drawn to a method for diagnosing the presence or activity of protein sequences of <i>C. diphtheriae</i> in a subject comprising detecting the presence of a nucleic acid sequence in the subject, classified in class 435, subclass 6. |

- Group VI: Claim 36, drawn to a host cell comprising a nucleic acid molecule wherein the nucleic acid molecule is disrupted, classified in class 435, subclass 252.3.
- Group VII: Claim 37, drawn to a host cell comprising a nucleic acid molecule wherein the nucleic acid molecule comprises one or more nucleic acid modifications, classified in class 435, subclass 252.3.
- Group VIII: Claim 38, drawn to a host cell comprising a nucleic acid molecule wherein the regulatory region of the nucleic acid molecule is modified relative to the wild-type regulatory region of the molecule, classified in class 435, subclass 252.3.

Applicants hereby elect, *without traverse*, Group I (claims 1-17) under 35 U.S.C. §121 for prosecution in the present application.

At paragraph 3 of the instant Restriction Requirement, the Examiner states that:

[t]he claims are generic to a plurality of disclosed patentably distinct species. Applicant is required under 35 U.S.C. 121 to elect a single disclosed species, even though this requirement is traversed. In the invention of Groups I-VIII, the species are each of the sequences listed in Tables 1-4, Appendix A and B, and SEQ ID NOs:1-1156. If any group is elected, Applicants must elect only one species for examination.

Applicants hereby elect SEQ ID NO:1, *with traverse*. Applicants further elect SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:7, SEQ ID NO:9, SEQ ID NO:11, SEQ ID NO:13, SEQ ID NO:15, SEQ ID NO:17, SEQ ID NO:21, and SEQ ID NO:23. Applicants respectfully submit that the policy set forth in 1192 O.G. 68 (Nov. 19, 1996), which the Examiner references, clearly provides that a **reasonable number** of sequences are allowed to be claimed in a single application. Ten sequences is a reasonable number of sequences to be examined in a single application. (M.P.E.P §803.04). Applicants respectfully submit that the claims, as amended, are directed to isolated nucleic acid molecule comprising the nucleotide sequence of any one of ten nucleotide sequences (SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:7, SEQ ID NO:9, SEQ ID NO:11, SEQ ID

NO:13, SEQ ID NO:15, SEQ ID NO:17, SEQ ID NO:21, and SEQ ID NO:23).

Accordingly, contrary to the Examiner's assertion that *any* DNA which encodes the disclosed polypeptides are claimed, the claims as amended are directed to ten nucleotide sequences.

Therefore, in the interest of saving considerable time and cost to Applicants and the United States Patent Office, and in accordance with 1192 O.G. 68 (Nov. 19, 1996), Applicants respectfully request that at least 10 sequences be examined in the instant application.

Furthermore, it is the Applicants' position that, with respect to the claimed nucleotide sequences, a species election for searching purposes would be more appropriate in this situation.

Applicants respectfully submit that a sufficient search and examination with respect to the claimed nucleotide sequences can be made without serious burden on the Examiner. As the M.P.E.P. states:

[i]f the search and examination of an entire application can be made without serious burden, the examiner must examine it on the merits, even though it includes claims to independent or distinct inventions. M.P.E.P. § 803.

Applicants respectfully submit that the searches with regard to each SEQ ID NO. would be co-extensive and would not involve a serious burden on the Examiner. Applicants therefore request that the Examiner re-characterize the restriction requirement with respect to the SEQ ID NOs. as a species election requirement.

It is the Applicants' understanding that under 35 U.S.C. §121, an election of a single species for prosecution on the merits is required, to which the claims will be restricted if no generic claim is finally held allowable. Applicants submits that claim 1 is generic. Applicants further understand that upon the allowance of a generic claim, Applicants will be entitled to consideration of claims to additional species which are written in dependent from or otherwise include all the limitations of an allowed generic claims as provided by 37 C.F.R. §1.41 *et seq.*

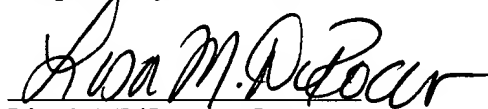
Accordingly, within Group I, Applicants hereby further elect the species of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:7, SEQ ID NO:9, SEQ ID NO:11, SEQ ID NO:13, SEQ ID NO:15, SEQ ID NO:17, SEQ ID NO:21, and SEQ ID NO:23 for search purposes only. Applicants even further elect the species of SEQ ID NO:1 for search purposes only.

Applicants reserve the right to traverse the above restriction with respect to non-elected Groups II-VIII in this or subsequent applications.

SUMMARY

If a telephone conversation with Applicants' Attorney would expedite the prosecution of the above-identified application, the examiner is urged to call the undersigned at (617) 227-7400.

Respectfully submitted,



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Dated: March 27, 2003

VERSION WITH MARKINGS TO SHOW CHANGES MADE

In the Claims:

Claims 1 and 3-7 have been amended as follows:

1. (Amended) An isolated nucleic acid molecule comprising the nucleotide sequence of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:7, SEQ ID NO:9, SEQ ID NO:11, SEQ ID NO:13, SEQ ID NO:15, SEQ ID NO:17, SEQ ID NO:21, or SEQ ID NO:23, or a complement thereof ~~from *Corynebacterium glutamicum* encoding a metabolic pathway protein, or a portion thereof,~~ provided that the nucleic acid molecule does not consist of any of the F-designated genes set forth in Table 1.

3. (Amended) An isolated *Corynebacterium glutamicum* nucleic acid molecule ~~selected from the group consisting of those sequences set forth in Appendix A, or a portion thereof,~~ provided that the nucleic acid molecule does not consist of any of the F-designated genes set forth in Table 1 comprising the nucleotide sequence of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:7, SEQ ID NO:9, SEQ ID NO:11, SEQ ID NO:13, SEQ ID NO:15, SEQ ID NO:17, SEQ ID NO:21, or SEQ ID NO:23, or the complement thereof.

4. (Amended) An isolated nucleic acid molecule which encodes a polypeptide ~~sequence selected from the group consisting of those sequences set forth in Appendix B,~~ provided that the nucleic acid molecule does not consist of any of the F-designated genes set forth in Table 1 comprising the amino acid sequence of SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:8, SEQ ID NO:10, SEQ ID NO:12, SEQ ID NO:14, SEQ ID NO:16, SEQ ID NO:18, SEQ ID NO:22, or SEQ ID NO:24.

5. (Amended) An isolated nucleic acid molecule which encodes a naturally occurring allelic variant of a polypeptide ~~selected from the group of amino acid sequences consisting of those sequences set forth in Appendix B,~~ provided that the nucleic acid molecule does not consist of any of the F-designated genes set forth in Table 1 comprising the amino acid sequence of SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:8, SEQ ID NO:10, SEQ ID NO:12, SEQ ID NO:14, SEQ ID NO:16, SEQ ID NO:18, SEQ ID NO:22, or SEQ ID NO:24, wherein the nucleic acid molecule hybridizes to the

complement of a nucleic acid molecule consisting of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:7, SEQ ID NO:9, SEQ ID NO:11, SEQ ID NO:13, SEQ ID NO:15, SEQ ID NO:17, SEQ ID NO:21, or SEQ ID NO:23, in 6X SSC at 45°C, followed by one or more washes in 0.2X SSC, 0.1% SDS at 50-65°C.

6. (Amended) An isolated nucleic acid molecule comprising a nucleotide sequence which ~~is at least 50% homologous to~~ has at least 50% identity with the a nucleotide sequence selected from the group consisting of those sequences set forth in Appendix A, or a portion thereof, provided that the nucleic acid molecule does not consist of any of the F-designated genes set forth in Table 1 of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:7, SEQ ID NO:9, SEQ ID NO:11, SEQ ID NO:13, SEQ ID NO:15, SEQ ID NO:17, SEQ ID NO:21, or SEQ ID NO:23, or the complement thereof.

7. (Amended) An isolated nucleic acid molecule comprising a fragment of at least 15 nucleotides of ~~a nucleic acid comprising a~~ the nucleotide sequence of selected from the group consisting of those sequences set forth in Appendix A, provided that the nucleic acid molecule does not consist of any of the F-designated genes set forth in Table 1 SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:7, SEQ ID NO:9, SEQ ID NO:11, SEQ ID NO:13, SEQ ID NO:15, SEQ ID NO:17, SEQ ID NO:21, or SEQ ID NO:23, or the complement thereof.

34. (Amended) A method for producing a fine chemical, comprising culturing a cell whose genomic DNA has been altered by the inclusion of a nucleic acid molecule of any one of claims 1-~~79~~.

APPENDIX A

1. An isolated nucleic acid molecule comprising the nucleotide sequence of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:7, SEQ ID NO:9, SEQ ID NO:11, SEQ ID NO:13, SEQ ID NO:15, SEQ ID NO:17, SEQ ID NO:21, or SEQ ID NO:23, or a complement thereof.

2. The isolated nucleic acid molecule of claim 1, wherein said metabolic pathway protein is selected from the group consisting of proteins involved in the metabolism of an amino acid, a vitamin, a cofactor, a nutraceutical, a nucleotide, a nucleoside, or trehalose.

3. An isolated *Corynebacterium glutamicum* nucleic acid molecule comprising the nucleotide sequence of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:7, SEQ ID NO:9, SEQ ID NO:11, SEQ ID NO:13, SEQ ID NO:15, SEQ ID NO:17, SEQ ID NO:21, or SEQ ID NO:23, or the complement thereof.

4. An isolated nucleic acid molecule which encodes a polypeptide comprising the amino acid sequence of SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:8, SEQ ID NO:10, SEQ ID NO:12, SEQ ID NO:14, SEQ ID NO:16, SEQ ID NO:18, SEQ ID NO:22, or SEQ ID NO:24.

5. An isolated nucleic acid molecule which encodes a naturally occurring allelic variant of a polypeptide comprising the amino acid sequence of SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:8, SEQ ID NO:10, SEQ ID NO:12, SEQ ID NO:14, SEQ ID NO:16, SEQ ID NO:18, SEQ ID NO:22, or SEQ ID NO:24, wherein the nucleic acid molecule hybridizes to the complement of a nucleic acid molecule consisting of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:7, SEQ ID NO:9, SEQ ID NO:11, SEQ ID NO:13, SEQ ID NO:15, SEQ ID NO:17, SEQ ID NO:21, or SEQ ID NO:23 in 6X SSC at 45°C, followed by one or more washes in 0.2X SSC, 0.1% SDS at 50-65°C.

6. An isolated nucleic acid molecule comprising a nucleotide sequence which has at least 50% identity with the nucleotide sequence of SEQ ID NO:1, SEQ ID

NO:3, SEQ ID NO:7, SEQ ID NO:9, SEQ ID NO:11, SEQ ID NO:13, SEQ ID NO:15, SEQ ID NO:17, SEQ ID NO:21, or SEQ ID NO:23, or the complement thereof.

7. An isolated nucleic acid molecule comprising a fragment of at least 15 nucleotides of the nucleotide sequence of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:7, SEQ ID NO:9, SEQ ID NO:11, SEQ ID NO:13, SEQ ID NO:15, SEQ ID NO:17, SEQ ID NO:21, or SEQ ID NO:23, or the complement thereof.

8. An isolated nucleic acid molecule which hybridizes to the nucleic acid molecule of any one of claims 1-7 under stringent conditions.

9. An isolated nucleic acid molecule comprising the nucleic acid molecule of claim 1 or a portion thereof and a nucleotide sequence encoding a heterologous polypeptide.

10. A vector comprising the nucleic acid molecule of claim 1.

11. The vector of claim 10, which is an expression vector.

12. A host cell transfected with the expression vector of claim 11.

13. The host cell of claim 12, wherein said cell is a microorganism.

14. The host cell of claim 13, wherein said cell belongs to the genus *Corynebacterium* or *Brevibacterium*.

15. The host cell of claim 12, wherein the expression of said nucleic acid molecule results in the modulation in production of a fine chemical from said cell.

16. The host cell of claim 15, wherein said fine chemical is selected from the group consisting of: organic acids, nonproteinogenic amino acids, purine and pyrimidine bases, nucleosides, nucleotides, lipids, saturated and unsaturated fatty acids, diols, carbohydrates, aromatic compounds, vitamins, cofactors, polyketides, and enzymes.

17. A method of producing a polypeptide comprising culturing the host cell of claim 12 in an appropriate culture medium to, thereby, produce the polypeptide.

18. An isolated metabolic pathway polypeptide from *Corynebacterium glutamicum*, or a portion thereof.

19. The protein of claim 18, wherein said polypeptide is selected from the group of metabolic pathway proteins which participate in the metabolism of an amino acid, a vitamin, a cofactor, a nutraceutical, a nucleotide, a nucleoside, or trehalose.

20. An isolated polypeptide comprising an amino acid sequence selected from the group consisting of those sequences set forth in Appendix B, provided that the amino acid sequence is not encoded by any of the F-designated genes set forth in Table 1.

21. An isolated polypeptide comprising a naturally occurring allelic variant of a polypeptide comprising an amino acid sequence selected from the group consisting of those sequences set forth in Appendix B, or a portion thereof, provided that the amino acid sequence is not encoded by any of the F-designated genes set forth in Table 1.

22. The isolated polypeptide of claim 18, further comprising heterologous amino acid sequences.

23. An isolated polypeptide which is encoded by a nucleic acid molecule comprising a nucleotide sequence which is at least 50% homologous to a nucleic acid selected from the group consisting of those sequences set forth in Appendix A, provided that the nucleic acid molecule does not consist of any of the F-designated nucleic acid molecules set forth in Table 1.

24. An isolated polypeptide comprising an amino acid sequence which is at least 50% homologous to an amino acid sequence selected from the group consisting of those sequences set forth in Appendix B, provided that the amino acid sequence is not encoded by any of the F-designated genes set forth in Table 1.

25. A method for producing a fine chemical, comprising culturing a cell containing a vector of claim 12 such that the fine chemical is produced.

26. The method of claim 25, wherein said method further comprises the step of recovering the fine chemical from said culture.

27. The method of claim 25, wherein said method further comprises the step of transfecting said cell with the vector of claim 11 to result in a cell containing said vector.

28. The method of claim 25, wherein said cell belongs to the genus *Corynebacterium* or *Brevibacterium*.

29. The method of claim 25, wherein said cell is selected from the group consisting of: *Corynebacterium glutamicum*, *Corynebacterium herculis*, *Corynebacterium lilium*, *Corynebacterium acetoacidophilum*, *Corynebacterium acetoglutamicum*, *Corynebacterium acetophilum*, *Corynebacterium ammoniagenes*, *Corynebacterium fujiokense*, *Corynebacterium nitrilophilus*, *Brevibacterium ammoniagenes*, *Brevibacterium butanicum*, *Brevibacterium divaricatum*, *Brevibacterium flavum*, *Brevibacterium healii*, *Brevibacterium ketoglutamicum*, *Brevibacterium ketosoreductum*, *Brevibacterium lactofermentum*, *Brevibacterium linens*, *Brevibacterium paraffinolyticum*, and those strains set forth in Table 3.

30. The method of claim 25, wherein expression of the nucleic acid molecule from said vector results in modulation of production of said fine chemical.

31. The method of claim 25, wherein said fine chemical is selected from the group consisting of: organic acids, nonproteinogenic amino acids, purine and pyrimidine bases, nucleosides, nucleotides, lipids, saturated and unsaturated fatty acids, diols, carbohydrates, aromatic compounds, vitamins, cofactors, polyketides, and enzymes.

32. The method of claim 25, wherein said fine chemical is an amino acid.

33. The method of claim 32, wherein said amino acid is drawn from the group consisting of: lysine, glutamate, glutamine, alanine, aspartate, glycine, serine, threonine, methionine, cysteine, valine, leucine, isoleucine, arginine, proline, histidine, tyrosine, phenylalanine, and tryptophan.

34. A method for producing a fine chemical, comprising culturing a cell whose genomic DNA has been altered by the inclusion of a nucleic acid molecule of any one of claims 1-7.

35. A method for diagnosing the presence or activity of *Corynebacterium diphtheriae* in a subject, comprising detecting the presence of one or more of the sequences set forth in Appendix A or Appendix B in the subject, provided that the sequences are not or are not encoded by any of the F-designated sequences set forth in Table 1, thereby diagnosing the presence or activity of *Corynebacterium diphtheriae* in the subject.

36. A host cell comprising a nucleic acid molecule selected from the group consisting of the nucleic acid molecules set forth in Appendix A, wherein the nucleic acid molecule is disrupted.

37. A host cell comprising a nucleic acid molecule selected from the group consisting of the nucleic acid molecules set forth in Appendix A, wherein the nucleic acid molecule comprises one or more nucleic acid modifications from the sequence set forth in Appendix A.

38. A host cell comprising a nucleic acid molecule selected from the group consisting of the nucleic acid molecules set forth in Appendix A, wherein the regulatory region of the nucleic acid molecule is modified relative to the wild-type regulatory region of the molecule.